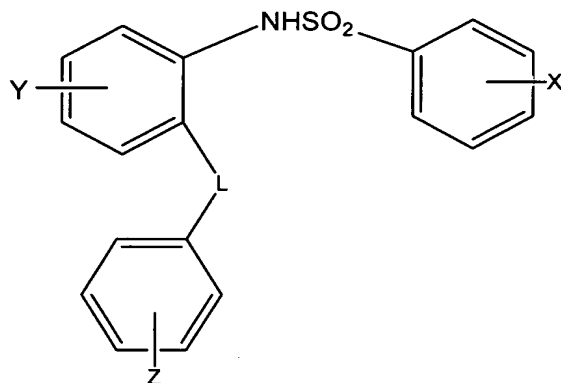


We claim:

1. A modulator of the formula (I) or a salt thereof:



where

L is -C(O)-, -S-, -S(O)- or -S(O)<sub>2</sub>-;

X represents from 1 to 4 substituents independently selected from the group consisting of halogen, -CN, -OH, -OR<sup>1</sup>, -C(O)R<sup>1</sup>, -CO<sub>2</sub>R<sup>1</sup>, -O(CO)R<sup>1</sup>, -C(O)NR<sup>1</sup>R<sup>2</sup>, -OC(O)NR<sup>1</sup>R<sup>2</sup>, -SR<sup>1</sup>, -SOR<sup>1</sup>, -SO<sub>2</sub>R<sup>1</sup>, -SO<sub>2</sub>NR<sup>1</sup>R<sup>2</sup>, -NR<sup>1</sup>R<sup>2</sup>, -NR<sup>1</sup>C(O)R<sup>2</sup>, -NR<sup>1</sup>C(O)<sub>2</sub>R<sup>2</sup>, -NR<sup>1</sup>SO<sub>2</sub>R<sup>2</sup>, -NR<sup>1</sup>(CO)NR<sup>1</sup>R<sup>2</sup>, unsubstituted C<sub>2-8</sub> alkyl, substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are each independently selected from the group consisting of hydrogen, unsubstituted or substituted C<sub>1-6</sub> alkyl, unsubstituted or substituted C<sub>3-6</sub> cycloalkyl, unsubstituted or substituted C<sub>2-6</sub> alkenyl, unsubstituted or substituted C<sub>2-6</sub> alkynyl, unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, unsubstituted or substituted aryl-C<sub>1-4</sub> alkyl, unsubstituted or substituted aryl-C<sub>1-4</sub> alkyl, and unsubstituted or substituted aryloxy-C<sub>1-4</sub> alkyl; or

two of  $R^1$ ,  $R^2$  and  $R^3$  together with the atom(s) to which they are attached, may form an unsubstituted or substituted 5-, 6- or 7-membered ring;

Y represents from 1 to 3 substituents, each independently selected from the group consisting of halogen, -CN, -OH, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -SR<sup>4</sup>, -SOR<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and unsubstituted or substituted C<sub>1-4</sub> alkyl;

$R^4$  is selected from the group consisting of hydrogen, unsubstituted or substituted C<sub>1-6</sub> alkyl, unsubstituted or substituted C<sub>3-6</sub> cycloalkyl, unsubstituted or substituted C<sub>2-6</sub> alkenyl, and unsubstituted or substituted C<sub>2-6</sub> alkynyl;

Z represents 0 to 5 substituents independently selected from the group consisting of halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>1-8</sub> alkoxy, =O, -CN, -NO<sub>2</sub>, -OH, -OR<sup>7</sup>, -OC(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -OC(O)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>C(O)R<sup>8</sup>, -NR<sup>7</sup>C(O)NR<sup>8</sup>R<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted heteroaryl and unsubstituted or substituted heterocyclyl; and

$R^7$ ,  $R^8$  and  $R^9$  are each independently hydrogen, unsubstituted or substituted C<sub>1-6</sub> alkyl, unsubstituted or substituted C<sub>3-6</sub> cycloalkyl, unsubstituted or substituted C<sub>2-6</sub> alkenyl, unsubstituted or substituted C<sub>2-6</sub> alkynyl, unsubstituted or substituted phenyl, unsubstituted or substituted heteroaryl, unsubstituted or substituted aryl-C<sub>1-4</sub> alkyl, and unsubstituted or substituted aryloxy-C<sub>1-4</sub> alkyl; or where any two of  $R^7$ ,  $R^8$  and  $R^9$  together with the atom(s) to which they are attached, may form a 5-, 6- or 7- membered ring.

2. The modulator of claim 1, where L is -CO-.
3. The modulator of claim 2, where X represents from 1 to 3 substituents independently selected from the group consisting of halogen, -CN, -OH, -OR<sup>1</sup>, -C(O)R<sup>1</sup>, -CO<sub>2</sub>R<sup>1</sup>, -O(CO)R<sup>1</sup>, -OC(O)NR<sup>1</sup>R<sup>2</sup>, -SR<sup>1</sup>, -SOR<sup>1</sup>, -SO<sub>2</sub>R<sup>1</sup>, -NR<sup>1</sup>R<sup>2</sup>, -

NR<sup>1</sup>C(O)R<sup>2</sup>, -NR<sup>1</sup>C(O)<sub>2</sub>R<sup>2</sup>, -NR<sup>1</sup>(CO)NR<sup>1</sup>R<sup>2</sup>, unsubstituted C<sub>2-8</sub> alkyl, substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted 5- or 6-membered heteroaryl, or unsubstituted or substituted 3- to 7-membered heterocyclyl.

4. The modulator of claim 2, where at least one X substituent is situated *para* to the sulfonamido bond as defined in formula (I).

5. The modulator of claim 2, where at least one X substituent is situated *meta* to the sulfonamido bond as defined in formula (I).

6. The modulator of claim 2, where at least one X substituent is situated *ortho* to the sulfonamido bond as defined in formula (I).

7. The modulator of claim 2, where at least one X is unsubstituted C<sub>2-8</sub> alkyl, unsubstituted C<sub>3-8</sub> cycloalkyl, unsubstituted C<sub>2-8</sub> alkenyl, or unsubstituted C<sub>2-8</sub> alkynyl.

8. The modulator of claim 2, where at least one X is substituted C<sub>1-8</sub> alkyl, substituted C<sub>3-8</sub> cycloalkyl, substituted C<sub>2-8</sub> alkenyl, or substituted C<sub>2-8</sub> alkynyl, each having from 1 to 5 substituents independently selected from the group consisting of halogen, -OH, -CN, -NO<sub>2</sub>, =O, -OC(O)R<sup>1</sup>, -OR<sup>1</sup>, -C(O)R<sup>1</sup>, -CONR<sup>1</sup>R<sup>2</sup>, -OC(O)NR<sup>1</sup>R<sup>2</sup>, -NR<sup>2</sup>C(O)R<sup>1</sup>, -NR<sup>1</sup>C(O)NR<sup>2</sup>R<sup>3</sup>, -CO<sub>2</sub>R<sup>1</sup>, -NR<sup>1</sup>R<sup>2</sup>, -NR<sup>2</sup>CO<sub>2</sub>R<sup>1</sup>, -SR<sup>1</sup>, -SOR<sup>1</sup>, -SO<sub>2</sub>R<sup>1</sup>, -SO<sub>2</sub>NR<sup>1</sup>R<sup>2</sup>, -NR<sup>1</sup>SO<sub>2</sub>R<sup>2</sup>, unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl.

9. The modulator of claim 8, where at least one X is substituted C<sub>1-8</sub> alkyl, having from 1 to 3 substituents independently selected from the group consisting of halogen, -OH, -CN, =O, -OC(O)R<sup>1</sup>, -OR<sup>1</sup>, -C(O)R<sup>1</sup>, -CONR<sup>1</sup>R<sup>2</sup>, -

$\text{NR}^2\text{C}(\text{O})\text{R}^1$ ,  $-\text{CO}_2\text{R}^1$ ,  $-\text{NR}^1\text{R}^2$ ,  $-\text{SO}_2\text{R}^1$ , unsubstituted or substituted phenyl, and unsubstituted or substituted 5- or 6-membered heteroaryl.

10. The modulator of claim 2, where at least one X is unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, or unsubstituted or substituted 3- to 10-membered heterocyclyl, where when X is substituted is has from 1 to 4 substituents independently selected from the group consisting of halogen, unsubstituted or substituted  $\text{C}_{1-8}$  alkyl,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{OH}$ ,  $-\text{OR}^1$ ,  $=\text{O}$ ,  $-\text{OC}(\text{O})\text{R}^1$ ,  $-\text{CO}_2\text{R}^1$ ,  $-\text{C}(\text{O})\text{R}^1$ ,  $-\text{CONR}^1\text{R}^2$ ,  $-\text{OC}(\text{O})\text{NR}^1\text{R}^2$ ,  $-\text{NR}^2\text{C}(\text{O})\text{R}^1$ ,  $-\text{NR}^1\text{C}(\text{O})\text{NR}^2\text{R}^3$ ,  $-\text{NR}^1\text{R}^2$ ,  $-\text{NR}^2\text{CO}_2\text{R}^1$ ,  $-\text{SR}^1$ ,  $-\text{SOR}^1$ ,  $-\text{SO}_2\text{R}^1$ ,  $-\text{SO}_2\text{NR}^1\text{R}^2$ , and  $-\text{NR}^1\text{SO}_2\text{R}^2$ .

11. The modulator of claim 10, where at least one X is unsubstituted or substituted phenyl, where when X is substituted it has from 1 to 3 substituents independently selected from the group consisting of halogen,  $-\text{OH}$ ,  $-\text{OR}^1$ ,  $-\text{C}(\text{O})\text{R}^1$ ,  $-\text{CONR}^1\text{R}^2$ ,  $-\text{NR}^2\text{C}(\text{O})\text{R}^1$ ,  $-\text{NR}^1\text{R}^2$ ,  $-\text{SO}_2\text{R}^1$ , and unsubstituted or substituted  $\text{C}_{1-8}$  alkyl.

12. The modulator of claim 10, where at least one X is unsubstituted or substituted 3- to 7-membered heterocyclyl, where when X is substituted it has from 1 to 3 substituents independently selected from the group consisting of  $\text{C}_{1-8}$  alkyl,  $-\text{OR}^1$ ,  $-\text{OH}$ ,  $-\text{OC}(\text{O})\text{R}^1$ ,  $-\text{CO}_2\text{R}^1$ ,  $-\text{C}(\text{O})\text{R}^1$ ,  $-\text{CONR}^1\text{R}^2$ ,  $-\text{NR}^1\text{R}^2$ ,  $-\text{SO}_2\text{R}^1$ , and  $-\text{NR}^1\text{SO}_2\text{R}^2$ .

13. The modulator of claim 10, where at least one X unsubstituted or substituted 5- or 6-membered heteroaryl, where when X is substituted it has from 1 to 3 substituents independently selected from the group consisting of halogen,  $-\text{OH}$ ,  $-\text{OR}^1$ ,  $-\text{C}(\text{O})\text{R}^1$ ,  $-\text{CONR}^1\text{R}^2$ ,  $-\text{NR}^2\text{C}(\text{O})\text{R}^1$ ,  $-\text{NR}^1\text{R}^2$ ,  $-\text{SO}_2\text{R}^1$ , and unsubstituted or substituted  $\text{C}_{1-8}$  alkyl.

14. The modulator of claim 2, where  $\text{R}^1$ ,  $\text{R}^2$  and  $\text{R}^3$ , when substituted, can have from 1 to 3 substituents independently selected from the group consisting of halogen,  $-\text{OH}$ ,  $-\text{OR}'$ ,  $-\text{OCOHNR}'$ ,  $-\text{OCONR}'_2$ ,  $-\text{SH}$ ,  $-\text{SR}'$ ,  $-\text{SO}_2\text{NH}_2$ ,  $-\text{CONH}_2$ ,  $-\text{NHC}(\text{O})\text{NH}_2$ ,  $\text{NR}'\text{C}(\text{O})\text{NH}_2$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CN}$ ,  $-\text{NO}_2$ ,  $-\text{NH}_2$ , -

NHR' and -NR'<sub>2</sub>, -S(O)R', -S(O)<sub>2</sub>R', -CO<sub>2</sub>R', -CONR'<sub>2</sub>, -CONHR', -C(O)R', -NR'COR', -NHCOR', -NR'CO<sub>2</sub>R', -NHCO<sub>2</sub>R', -CO<sub>2</sub>R', -NR'C(O)NR'<sub>2</sub>, -NHC(O)NR'<sub>2</sub>, -NR'C(O)NHR', -NHC(O)NHR', -NR'SO<sub>2</sub>R', -NH<sub>2</sub>SO<sub>2</sub>R', -SO<sub>2</sub>NR'<sub>2</sub>, and -SO<sub>2</sub>NHR', where R' is C<sub>1-6</sub>alkyl.

15. The modulator of claim 2, where Y represents from 1 to 3 substituents independently selected from the group consisting of halogen, -CN, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -SR<sup>4</sup>, -CF<sub>3</sub>, -SOR<sup>4</sup>, and -SO<sub>2</sub>R<sup>4</sup>.

16. The modulator of claim 15, where Y represents from 1 to 3 substituents independently selected from the group consisting of halogen, -CN, -CF<sub>3</sub>, and -SO<sub>2</sub>R<sup>4</sup>.

17. The modulator of claim 15, where at least one Y represents halogen.

18. The modulator of claim 2, where Y represents from 1 to 2 substituents, each independently selected from the group consisting of halogen, -CN, -OH, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -SR<sup>4</sup>, -SOR<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and unsubstituted or substituted C<sub>1-4</sub> alkyl.

19. The modulator of claim 18, where one Y represents a halogen and another substituent selected from the group consisting of halogen, -CN, -OH, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -SR<sup>4</sup>, -SOR<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup> and unsubstituted or substituted C<sub>1-4</sub> alkyl.

20. The modulator of claim 18, where at least one Y substituent is located *para* to the sulfonamide bond as defined in formula (I) and another Y substituent is halogen.

21. The modulator of claim 15, where at least one Y is unsubstituted C<sub>1-4</sub> alkyl.

22. The modulator of claim 15, where at least one Y is substituted C<sub>1-4</sub> alkyl, having from 1 to 3 substituents independently selected from the group consisting of halogen, -OH, -OR<sup>4</sup>, -CN, -NO<sub>2</sub>, =O, -OC(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -

$C(O)R^4$ ,  $-CONR^4R^5$ ,  $-OC(O)NR^4R^5$ ,  $-NR^4C(O)R^5$ ,  $-NR^4C(O)NR^5R^6$ ,  $-NR^4R^5$ ,  $-NR^4CO_2R^5$ ,  $-SR^4$ ,  $-SOR^4$ ,  $-SO_2R^4$ ,  $-SO_2NR^4R^5$ , and  $-NR^4SO_2R^5$ ,

where  $R^4$ ,  $R^5$  and  $R^6$  are each independently selected from the group consisting of hydrogen, unsubstituted or substituted  $C_{1-6}$  alkyl, unsubstituted or substituted  $C_{3-6}$  cycloalkyl, unsubstituted or substituted  $C_{2-6}$  alkenyl, and unsubstituted or substituted  $C_{2-6}$  alkynyl; or where any two of  $R^4$ ,  $R^5$  and  $R^6$  together with the atom(s) to which they are attached, may form a 5-, 6- or 7-membered ring.

23. The modulator of claim 22, where at least one Y is substituted  $C_{1-4}$  alkyl, having from 1 to 3 substituents independently selected from the group consisting of halogen,  $-OH$ ,  $-OR^4$ ,  $-CN$ ,  $-NO_2$ ,  $=O$ ,  $-OC(O)R^4$ ,  $-CO_2R^4$ ,  $-C(O)R^4$ ,  $-CONR^4R^5$ ,  $-NR^4C(O)R^5$ ,  $-NR^4R^5$ ,  $-NR^4$ ,  $-SR^4$ ,  $-SOR^4$ ,  $-SO_2R^4$ , and  $-NR^4SO_2R^5$ .

24. The modulator of claim 23, where  $R^4$ ,  $R^5$  and  $R^6$ , when substituted, can have from with from 1 to 3 substituents independently selected from the group consisting of halogen,  $-OH$ ,  $-OR'$ ,  $-SH$ ,  $-SR'$ ,  $-SO_2NH_2$ ,  $-CONH_2$ ,  $-NHC(O)NH_2$ ,  $N(C_{1-6}alkyl)C(O)NH_2$ ,  $-CO_2H$ ,  $-CN$ ,  $-NO_2$ ,  $-NH_2$ ,  $-NHR'$ ,  $-NR'_2$ ,  $-S(O)R'$ ,  $-S(O)_2R'$ ,  $-CO_2R'$ ,  $-CONHR'$ ,  $-CONR'_2$ , and  $-C(O)R'$ , where  $R'$  is  $C_{1-6}alkyl$ .

25. The modulator of claim 2, where Z represents 0 to 3 substituents independently selected from the group consisting of halogen, unsubstituted or substituted  $C_{1-8}$  alkyl, unsubstituted or substituted  $C_{3-8}$  cycloalkyl, unsubstituted or substituted  $C_{2-8}$  alkenyl, unsubstituted or substituted  $C_{2-8}$  alkynyl, unsubstituted or substituted  $C_{1-8}$  alkoxy,  $=O$ ,  $-CN$ ,  $-NO_2$ ,  $-OH$ ,  $-OR^7$ ,  $-OC(O)R^7$ ,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-CONR^7R^8$ ,  $-NR^7C(O)R^8$ ,  $-NR^7R^8$ ,  $-SR^7$ ,  $-SOR^7$ ,  $-SO_2R^7$ ,  $-SO_2NR^7R^8$ ,  $-NR^7SO_2R^8$ , unsubstituted or substituted phenyl, unsubstituted or substituted 5- or 6-membered heteroaryl, and unsubstituted or substituted 3- to 7-membered heterocyclyl.

26. The modulator of claim 2, where Z represents 0 to 2 substituents independently selected from the group consisting of halogen, unsubstituted or substituted C<sub>1-6</sub> alkyl, unsubstituted or substituted C<sub>1-6</sub> alkoxy, =O, -CN, -NO<sub>2</sub>, -OH, -OR<sup>7</sup>, -C(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>C(O)R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, unsubstituted or substituted phenyl, unsubstituted or substituted 3 to 7-membered heterocyclyl, and unsubstituted or substituted 5- or 6-membered heteroaryl.

27. The modulator of claim 25, where at least one Z is unsubstituted C<sub>1-8</sub> alkyl, unsubstituted C<sub>3-8</sub> cycloalkyl, unsubstituted C<sub>2-8</sub> alkenyl, unsubstituted C<sub>2-8</sub> alkynyl or unsubstituted C<sub>1-8</sub> alkoxy, unsubstituted 6- to 10-membered aryl, unsubstituted 3- to 7-membered heterocyclyl, and 3- to 7-membered heteraryl.

28. The modulator of claim 25, where at least one Z is substituted C<sub>1-8</sub> alkyl, substituted C<sub>3-8</sub> cycloalkyl, substituted C<sub>2-8</sub> alkenyl, substituted C<sub>2-8</sub> alkynyl or substituted C<sub>1-8</sub> alkoxy, each having from 1 to 5 substituents independently selected from the group consisting of halogen, -OH, -OR<sup>7</sup>, -CN, -NO<sub>2</sub>, =O, -CN, -NO<sub>2</sub>, -OC(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -OC(O)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>C(O)R<sup>8</sup>, -NR<sup>7</sup>C(O)NR<sup>8</sup>R<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, unsubstituted or substituted phenyl, unsubstituted or substituted 5- or 6- membered heteroaryl, or unsubstituted or substituted 3- to 6-membered heterocyclyl.

29. The modulator of claim 25, where each R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup>, when substituted, can have from 1 to 3 substituents independently selected from the group consisting of halogen, -OH, -OR', -OCONHR', -OCONR'<sub>2</sub>, -SH, -SR', -CN, -SO<sub>2</sub>NH<sub>2</sub>, -CONH<sub>2</sub>, -NHC(O)NH<sub>2</sub>, -NR'C(O)NH<sub>2</sub>, -CO<sub>2</sub>H, -NO<sub>2</sub>, -NH<sub>2</sub>, -NHR' and -NR'<sub>2</sub>, -S(O)R', -S(O)<sub>2</sub>R', -CO<sub>2</sub>R', -CONR'<sub>2</sub>, -CONHR', -C(O)R', -NR'COR', -NHCOR', -NR'CO<sub>2</sub>R', -NHCO<sub>2</sub>R', -CO<sub>2</sub>R', -NR'C(O)NR'<sub>2</sub>, -NHC(O)NR'<sub>2</sub>, -NR'C(O)NHR', -NHC(O)NHR', -NR'SO<sub>2</sub>R', -NHSO<sub>2</sub>R', -SO<sub>2</sub>NR'<sub>2</sub>, and -SO<sub>2</sub>NHR', where R' is C<sub>1-6</sub>alkyl.

30. The modulator of claim 3, where Y represents from 1 to 3 substituents, each independently selected from the group consisting of halogen, -CN, -OH, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -SR<sup>4</sup>, -SOR<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and unsubstituted or substituted C<sub>1-4</sub> alkyl.

31. The modulator of claim 30, where at least one Y is halogen.

32. The modulator of claim 25, where Y represents from 1 to 3 substituents, each independently selected from the group consisting of halogen, -CN, -OH, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -SR<sup>4</sup>, -SOR<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and unsubstituted or substituted C<sub>1-4</sub> alkyl.

33. The modulator of claim 32, where at least one Y is halogen.

34. The modulator of claim 15, where Z represents 0 to 3 substituents independently selected from the group consisting of halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>1-8</sub> alkoxy, =O, -CN, -NO<sub>2</sub>, -OH, -OR<sup>7</sup>, -OC(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>C(O)R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, unsubstituted or substituted phenyl, unsubstituted or substituted 5- or 6-membered heteroaryl, and unsubstituted or substituted 3- to 7-membered heterocyclyl.

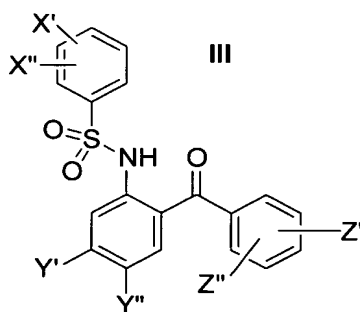
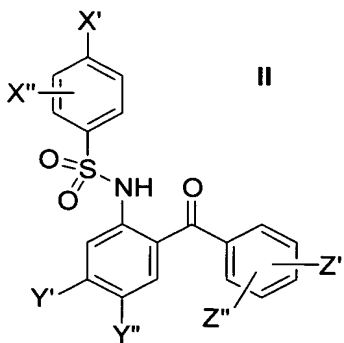
35. The modulator of claim 34, where X is unsubstituted C<sub>2-8</sub> alkyl or substituted C<sub>1-8</sub> alkyl.

36. The modulator of claim 34, where at least one Y is halogen.

37. The modulator of claim 30, where Z represents 0 to 3 substituents independently selected from the group consisting of halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>1-8</sub> alkoxy, =O, -CN, -NO<sub>2</sub>, -OH, -OR<sup>7</sup>, -OC(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>C(O)R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -

$\text{SO}_2\text{R}^7$ ,  $-\text{SO}_2\text{NR}^7\text{R}^8$ ,  $-\text{NR}^7\text{SO}_2\text{R}^8$ , unsubstituted or substituted phenyl, unsubstituted or substituted 5- or 6-membered heteroaryl, and unsubstituted or substituted 3- to 7-membered heterocyclyl.

38. The modulator of claim 37, where X is unsubstituted  $\text{C}_{2-8}$  alkyl or substituted  $\text{C}_{1-8}$  alkyl.
39. The modulator of claim 37, where at least one Y is halogen.
40. The modulator of claim 1, which has activity in a chemotaxis assay of  $<10000$  nM.
41. The modulator of claim 1, which has activity in a chemotaxis assay of  $<1000$  nM.
42. The modulator of claim 1, which has activity in a chemotaxis assay of  $<100$  nM.
43. The modulator of claim 1, which has activity in a CCR9 chemotaxis assay of  $<10000$  nM.
44. The modulator of claim 1, which has activity in a CCR9 chemotaxis assay of  $<1000$  nM.
45. The modulator of claim 1, which has activity in a CCR9 chemotaxis assay of  $<100$  nM.
46. A modulator of one of the formulae (II) or (III) or a salt thereof:



where X' and X'' are each independently selected from the group consisting of hydrogen, halogen, -CN, -OH, -OR<sup>1</sup>, -C(O)R<sup>1</sup>, -CO<sub>2</sub>R<sup>1</sup>, -O(CO)R<sup>1</sup>, -C(O)NR<sup>1</sup>R<sup>2</sup>, -OC(O)NR<sup>1</sup>R<sup>2</sup>, -SR<sup>1</sup>, -SOR<sup>1</sup>, -SO<sub>2</sub>R<sup>1</sup>, -SO<sub>2</sub>NR<sup>1</sup>R<sup>2</sup>, -NR<sup>1</sup>R<sup>2</sup>, -NR<sup>1</sup>C(O)R<sup>2</sup>, -NR<sup>1</sup>C(O)<sub>2</sub>R<sup>2</sup>, -NR<sup>1</sup>SO<sub>2</sub>R<sup>2</sup>, -NR<sup>1</sup>(CO)NR<sup>2</sup>R<sup>3</sup>, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted 6- to 10-membered aryl, unsubstituted or substituted 5- to 10-membered heteroaryl, and unsubstituted or substituted 3- to 10-membered heterocyclyl, with the proviso that if one of X' and X'' is hydrogen than the other is not hydrogen or unsubstituted methyl;

R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are each independently selected from the group consisting of hydrogen, C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, 6- to 10-membered aryl, 5- to 10-membered heteroaryl, aryl-C<sub>1-4</sub> alkyl, aryl-C<sub>1-4</sub> alkyl, and aryloxy-C<sub>1-4</sub> alkyl; or

two of R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> together with the atom(s) to which they are attached, may form a 5-, 6- or 7- membered ring;

Y' and Y'' are each independently selected from the group consisting of hydrogen, halogen, -CN, -OH, -OR<sup>4</sup>, -C(O)R<sup>4</sup>, -CO<sub>2</sub>R<sup>4</sup>, -SR<sup>4</sup>, -SOR<sup>4</sup>, -SO<sub>2</sub>R<sup>4</sup>, and unsubstituted or substituted C<sub>1-4</sub> alkyl, with the proviso that Y' and Y'' cannot both be hydrogen simultaneously;

R<sup>4</sup> is selected from the group consisting of hydrogen, unsubstituted or substituted C<sub>1-6</sub> alkyl, unsubstituted or substituted C<sub>3-6</sub> cycloalkyl, unsubstituted or substituted C<sub>2-6</sub> alkenyl, and unsubstituted or substituted C<sub>2-6</sub> alkynyl;

Z' and Z'' are each independently selected from the group consisting of hydrogen, halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, unsubstituted or substituted C<sub>2-8</sub> alkenyl, unsubstituted or substituted C<sub>2-8</sub> alkynyl, unsubstituted or substituted C<sub>1-8</sub> alkoxy, =O, -CN, -NO<sub>2</sub>, -OH, -OR<sup>7</sup>, -OC(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -OC(O)NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>C(O)R<sup>8</sup>, -NR<sup>7</sup>C(O)NR<sup>8</sup>R<sup>9</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, unsubstituted or substituted 6- to

10-membered aryl, unsubstituted or substituted 5- or 6-membered heteroaryl and unsubstituted or substituted 3- to 7-membered heterocyclyl; and

where  $R^7$ ,  $R^8$  and  $R^9$  are each independently hydrogen, unsubstituted or substituted  $C_{1-6}$  alkyl, unsubstituted or substituted  $C_{3-6}$  cycloalkyl, unsubstituted or substituted  $C_{2-6}$  alkenyl, unsubstituted or substituted  $C_{2-6}$  alkynyl, unsubstituted or substituted phenyl, unsubstituted or substituted heteroaryl, unsubstituted or substituted aryl- $C_{1-4}$  alkyl, and unsubstituted or substituted aryloxy- $C_{1-4}$  alkyl; or where any two of  $R^7$ ,  $R^8$  and  $R^9$  together with the atom(s) to which they are attached, may form a 5-, 6- or 7- membered ring.

47. The modulator of claim 46, where  $X'$  and  $X''$  are each independently selected from the group consisting of hydrogen, halogen, -CN, -OR<sup>1</sup>, -C(O)R<sup>1</sup>, -SO<sub>2</sub>R<sup>1</sup>, -NR<sup>1</sup>R<sup>2</sup>, unsubstituted or substituted  $C_{1-8}$  alkyl, unsubstituted or substituted  $C_{3-8}$  cycloalkyl, unsubstituted or substituted  $C_{2-8}$  alkenyl, unsubstituted or substituted phenyl, unsubstituted or substituted 5- or 6-membered heteroaryl, unsubstituted or substituted 5- or 6-membered heterocyclyl, with the proviso that if one of  $X'$  and  $X''$  is hydrogen than the other is not hydrogen or unsubstituted methyl.

48. The modulator of claim 46, where  $X'$  and  $X''$  are each independently selected from the group consisting of hydrogen, halogen, -CN, -CF<sub>3</sub>, -CH=CH<sub>2</sub>, isoamyl, phenylacetylene, t-butyl, ethyl (Et), i-propyl (<sup>i</sup>Pr), -C(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, hydroxybutyl, -C(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me, -OCF<sub>3</sub>, -OMe, -O<sup>i</sup>Pr, -C(O)Me, -SO<sub>2</sub>Me, phenyl (Ph), -OEt, pyrazole, thiophene, aminopyridine, oxazole, and morpholinyl, with the proviso that  $X'$  and  $X''$  cannot both be hydrogen simultaneously.

49. The modulator of claim 46, where  $Y'$  and  $Y''$  are each independently hydrogen or halogen, with the proviso that one or both are halogen.

50. The modulator of claim 46, where  $Y'$  is hydrogen and  $Y''$  is chloro or bromo.

51. The modulator of claim 46, where at least one of Y' or Y'' is a halogen atom and is *ortho* to the sulfonamide bond in formula (I).
52. The modulator of claim 46, where at least one of Y' or Y'' is a halogen atom and is *meta* to the sulfonamide bond in formula (I).
53. The modulator of claim 46, where at least one of Y' or Y'' is a halogen atom and is *para* to the sulfonamide bond in formula (I).
54. The modulator of claim 46, where Z' and Z'' are each independently selected from the group consisting of hydrogen, halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, -CN, -OH, -OR<sup>7</sup>, -C(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -OC(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, unsubstituted or substituted phenyl, and unsubstituted or substituted 5- or 6-membered heteroaryl, unsubstituted or substituted 3- to 7-membered heterocycyl.
55. The modulator of claim 46, where Z' and Z'' are each independently hydrogen, halogen, -CN, -OR<sup>7</sup>, -NR<sup>7</sup>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, and -SO<sub>2</sub>R<sup>7</sup>, unsubstituted or substituted C<sub>1-6</sub> alkoxyl, unsubstituted or substituted C<sub>1-6</sub> alkyl, unsubstituted or substituted phenyl, or unsubstituted or substituted 5- or 6-membered heterocyclyl.
56. The modulator of claim 47, where Y' and Y'' are each independently hydrogen or halogen, with the proviso that one or both are halogen.
57. The modulator of claim 47, where Z' and Z'' are each independently selected from the group consisting of hydrogen, halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, -CN, -OH, -OR<sup>7</sup>, -C(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -OC(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, unsubstituted or substituted phenyl, and unsubstituted or substituted 5- or 6-membered heteroaryl, unsubstituted or substituted 3- to 7-membered heterocycyl.

58. The modulator of claim 49, where Z' and Z'' are each independently selected from the group consisting of hydrogen, halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>1-8</sub> cycloalkyl, -CN, -OH, -OR<sup>7</sup>, -C(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -OC(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, unsubstituted or substituted 6- to 10-membered aryl, and unsubstituted or substituted 5- or 6-membered heteroaryl, unsubstituted or substituted 3- to 7-membered heterocycyl.

59. The modulator of claim 56, where Z' and Z'' are each independently selected from the group consisting of hydrogen, halogen, unsubstituted or substituted C<sub>1-8</sub> alkyl, unsubstituted or substituted C<sub>3-8</sub> cycloalkyl, -CN, -OH, -OR<sup>7</sup>, -C(O)R<sup>7</sup>, -CO<sub>2</sub>R<sup>7</sup>, -OC(O)R<sup>7</sup>, -CONR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>R<sup>8</sup>, -NR<sup>7</sup>CO<sub>2</sub>R<sup>8</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -NR<sup>7</sup>SO<sub>2</sub>R<sup>8</sup>, -SO<sub>2</sub>NR<sup>7</sup>R<sup>8</sup>, unsubstituted or substituted phenyl, and unsubstituted or substituted 5- or 6-membered heteroaryl, unsubstituted or substituted 3- to 7-membered heterocycyl.

60. A composition comprising a pharmaceutically acceptable carrier and a compound of claim 2.

61. A method for treating a CCR9-mediated condition or disease comprising administering to a subject a safe and effective amount of The modulator of claim 2.

62. The method of claim 61, where the CCR9-mediated disease or condition is an inflammatory condition, an immunoregulatory disorder.

63. The method of claim 61, where the CCR9-mediated disease or condition is inflammatory bowel disease, an allergic disease, psoriasis, atopic dermatitis, asthma, fibrotic diseases, graft rejection, immune mediated food allergies, autoimmune diseases, Celiac disease, rheumatoid arthritis, thymoma, thymic carcinoma, leukemia, solid tumor, or acute lymphocytic leukemia.

64. The method of claim 61, further comprising administering an anti-inflammatory or analgesic agent.
65. The method of claim 61, where the administering is oral, parenteral, rectal, transdermal, sublingual, nasal or topical.
66. The method of claim 61, where the compound is administered in combination with an anti-inflammatory or analgesic agent.
67. A method of modulating CCR9 function in a cell, comprising contacting the cell with a CCR9 modulating amount of the modulator of claim 2.